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09/165,460	10/02/98	RINE J	B96-021-3

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RICHARD ARON OSMAN
SCIENCE AND TECHNOLOGY LAW GROUP
75 DENISE DRIVE
HILLSBOROUGH CA 94010

EXAMINER	
TUNG, P	
ART UNIT	PAPER NUMBER
1652	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No. 09/165,460	Applicant(s) Rine et al.
	Examiner Peter Tung	Group Art Unit 1652

☒ Responsive to communication(s) filed on *Jan 2, 2001* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *31-46* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *31-46* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 31-46 are pending.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant expression vector comprising a polynucleotide which hybridizes to a nucleic acid which encodes a polypeptide of SEQ ID NO: 2 and wherein the polynucleotide contained on the expression vector encodes a polypeptide which the proteolytic removal of an AAX tripeptide from a prenylated CAAX protein, does not reasonably provide enablement for a recombinant expression vector comprising a polynucleotide which hybridizes to a nucleic acid which encodes a polypeptide of SEQ ID NO: 2 or conservatively modified SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of

working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The breadth of the claim encompasses a recombinant expression vector comprising any polynucleotide which hybridizes to either a nucleic acid which encodes a polypeptide consisting of SEQ ID NO: 2 or a nucleic acid which encodes a polypeptide consisting of conservatively modified SEQ ID NO: 2. Insufficient guidance and examples are provided on an expression vector comprising a polynucleotide which hybridizes with a nucleic acid encoding SEQ ID NO: 2 wherein the polynucleotide contained on the expression vector does not encode a polypeptide having said proteolytic activity. As there is unpredictability in hybridization such that a polynucleotide which hybridizes to a polynucleotide encoding SEQ ID NO: 2 would not necessarily encode SEQ ID NO: 2 or a polypeptide with said proteolytic activity. The skill of those in the art is low in using a polynucleotides which hybridizes to a nucleic acid encoding SEQ ID NO: 2 but which does not encode either SEQ ID NO: 2 or a polypeptide having said protease activity. Insufficient guidance and examples are provided of a conservatively modified SEQ ID NO: 2 which has said proteolytic activity. Insufficient guidance and examples are provided of where conservative modifications can be made to SEQ ID NO: 2 without affecting its enzymatic function. The breadth of the claim encompasses any conservative modifications. As there is unpredictability in the art in making even conservative substitutions in a protein sequence without affecting its structure and function, the level of skill in the art is low in making a polynucleotide which would hybridize to a nucleic acid encoding a conservatively modified SEQ ID NO: 2.

Undue experimentation would be required to enable the full scope of the claims based upon the limited scope of the disclosure.

4. Claims 35-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant expression vector comprising a polynucleotide which hybridizes to a nucleic acid which encodes a polypeptide of SEQ ID NO: 4 and wherein the polynucleotide contained on the expression vector encodes a polypeptide which the proteolytic removal of an AAX tripeptide from a prenylated CAAX protein, does not reasonably provide enablement for a recombinant expression vector comprising a polynucleotide which hybridizes to a nucleic acid which encodes a polypeptide of SEQ ID NO: 4 or conservatively modified SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The breadth of the claim encompasses a recombinant expression vector comprising any polynucleotide which hybridizes to either a nucleic acid which encodes a polypeptide consisting of SEQ ID NO: 4 or a nucleic acid which encodes a polypeptide consisting of

conservatively modified SEQ ID NO: 4. Insufficient guidance and examples are provided on an expression vector comprising a polynucleotide which hybridizes with a nucleic acid encoding SEQ ID NO: 4 wherein the polynucleotide contained on the expression vector does not encode a polypeptide having said proteolytic activity. As there is unpredictability in hybridization such that a polynucleotide which hybridizes to a polynucleotide encoding SEQ ID NO: 4 would not necessarily encode SEQ ID NO: 4 or a polypeptide with said proteolytic activity. The skill of those in the art is low in using a polynucleotides which hybridizes to a nucleic acid encoding SEQ ID NO: 4 but which does not encode either SEQ ID NO: 4 or a polypeptide having said protease activity. Insufficient guidance and examples are provided of a conservatively modified SEQ ID NO: 4 which has said proteolytic activity. Insufficient guidance and examples are provided of where conservative modifications can be made to SEQ ID NO: 4 without affecting its enzymatic function. The breadth of the claim encompasses any conservative modifications. As there is unpredictability in the art in making even conservative substitutions in a protein sequence without affecting its structure and function, the level of skill in the art is low in making a polynucleotide which would hybridize to a nucleic acid encoding a conservatively modified SEQ ID NO: 4. Undue experimentation would be required to enable the full scope of the claims based upon the limited scope of the disclosure.

5. Applicants argue that one does not need to know, a priori, the functional impact of any proposed conservative substitution as the art provides convenient screening methods to confirm

retention of the required protease activity. Applicants argue that the screening is routine and within the bounds of experimentation permitted by 35 U.S.C. 112 1st paragraph.

6. Applicant's arguments filed 1/23/01 have been fully considered but they are not persuasive. As stated in the previous Office action, several factors are to be considered in determining whether a disclosure would require undue experimentation. While a screening method may be provided, screening the many conservative variations of SEQ ID NO: 2 and 4 encompassed by the breadth of the claim would require undue experimentation. Insufficient guidance is provided on where conservative changes can be made. A large amount of experimentation would also be required to make the conservative variations encompassed by the claims.

7. Claims 31-33, 35-37, 39-41 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a vector comprising a polynucleotide hybridizing to a nucleic acid encoding SEQ ID NO: 2 or 4 or conservatively modified SEQ ID NO: 2 or 4 and transformed host cells comprising said vectors. However, only the polypeptide sequence of SEQ ID NO: 2 and 4 and the DNA sequence of SEQ ID NO: 1 and 2 have been disclosed. The specification and claims do not indicate what distinguishing attributes are shared by the members of the claimed genus of a vector comprising a polynucleotide hybridizing to a nucleic acid encoding SEQ ID NO: 2 or 4 or conservatively modified SEQ ID NO: 2 or 4. The scope of the claim includes numerous chemical species with

widely differing structural, chemical and physical characteristics and the genus is highly variable because a significant number of structural differences between genus members is permitted. The specification and the claims do not provide any guidance as to what is essential to the operation and function of the claimed a vector comprising a polynucleotide hybridizing to a nucleic acid encoding SEQ ID NO: 2 or 4 or conservatively modified SEQ ID NO: 2 or 4 and what characteristics could distinguish compounds in the genus from others in the genus are missing from the disclosure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variable, a single disclosed member of the genus is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus of a vector comprising a polynucleotide hybridizing to a nucleic acid encoding conservatively modified SEQ ID NO: 2 or 4. *see University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

8. Applicants argue that due to the degeneracy of the genetic code, any number of sequences which encode the recited polypeptide are possible. Similarly for those sequences that hybridize, any number of sequences are possible.

9. Applicant's arguments filed 1/23/01 have been fully considered but they are not persuasive. As claimed, the instant polynucleotides which hybridize to said nucleic acid sequence are not limited so that said polynucleotide encodes a polypeptide with the proteolytic activity of the reference polypeptide.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 31-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 31 and 35 are indefinite as the specific conditions specified for the high stringency hybridization are not provided.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 31-34 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al. in view of Nozaki et al. (U.S. Patent No. 4,997,767). Rose et al. teach a polynucleotide identical to SEQ ID NO: 1 and which encodes SEQ ID NO: 2. Such a polynucleotide sequence would be expected to hybridize to a polynucleotide encoding SEQ ID NO: 2 under stringent conditions. Rose et al. do not teach a vector comprising said sequence or host cells comprising said vector. Nozaki et al. teach (Col. 2, lines 45 to Col. 3, line 60) a yeast shuttle vector for expressing proteins in yeast which can replicate in both E. coli and in yeast. Nozaki et al. do not teach a vector comprising a polynucleotide which hybridizes to a polynucleotide encoding SEQ ID NO: 2 or prokaryotic and yeast cells transformed with said vector. It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce vectors, as taught by Nozaki et al., comprising the polynucleotide taught by Rose et al., for the benefit of replicating said vector in E. coli and transforming yeast with said vectors and thereby obtaining yeast for expression of the protein encoded by the DNA taught by Rose et al. One of ordinary skill in the art is motivated to combine the two references as Nozaki et al. teaches a vector for expressing proteins in yeast where the vector can also replicate in E. coli. Rose et al. teach a DNA sequence which encodes a protein where said DNA sequence can be used in the vector taught by Nozaki et al. One of ordinary skill in the art would have a reasonable expectation of success at doing this as the use of shuttle vectors for replicating DNA and

expression is well known in the art. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

15. Claims 35-38 and 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lye et al. in view of Nozaki et al. (U.S. Patent No. 4,997,767). Lye et al. teach a polynucleotide (complement of 25838-26785 of SC8156) identical to SEQ ID NO: 3 and which encodes SEQ ID NO: 4. Such a polynucleotide sequence would be expected to hybridize to a polynucleotide encoding SEQ ID NO: 4 under stringent conditions. Lye et al. do not teach a vector comprising said sequence or host cells comprising said vector. Nozaki et al. teach (Col. 2, lines 45 to Col. 3, line 60) a yeast shuttle vector for expressing proteins in yeast which can replicate in both E. coli and in yeast. Nozaki et al. do not teach a vector comprising a polynucleotide which hybridizes to a polynucleotide encoding SEQ ID NO: 4 or prokaryotic and yeast cells transformed with said vector. It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce vectors, as taught by Nozaki et al., comprising the polynucleotide taught by Lye et al., for the benefit of replicating said vector in E. coli and transforming yeast with said vectors and thereby obtaining yeast for expression of the protein encoded by the DNA taught by Lye et al. One of ordinary skill in the art is motivated to combine the two references as Nozaki et al. teaches a vector for expressing proteins in yeast where the vector can also replicate in E. coli. Lye et al teach a DNA sequence which encodes a protein where said DNA sequence can be used in the vector taught by Nozaki et al. One of ordinary skill in the art would have a reasonable expectation of success at doing this as the use of shuttle vectors for replicating DNA and

expression is well known in the art. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

16. Applicants argue that Rose et al. is not prior art as it has a date of Aug. 11, 1997 and that the "creation date" for the reference of Oct. 6, 1995 is not the date at which the reference was published. Applicants argue that the evidence dictates that the reference purportedly created on Aug. 11, 1997 is not the same as that created on Oct. 6, 1995. Applicants further argue that with no evidence for function for the relevant yeast ORFs, there would be no motivation to select out any specific ORF of unknown function, isolate out what may or may not be a coding sequence and operatively join it to a promoter.

17. Applicant's arguments with respect to claims 12,17,18,22 and 23 have been considered but are moot in view of the new ground(s) of rejection. Applicants have not provided any evidence that Rose et al. was not publicly available as of the creation date of Oct. 6, 1995. Additionally, no evidence is provided that changes between the document dated Aug. 11, 1997 and that created on Oct. 6, 1995 affect the use of the document as prior art.

While no function may be given to a putative open reading, what nucleotides constitute an open reading frame are identified in the prior art. and one would express an unknown protein in order to characterize it.

Conclusion

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, Ph.D., can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600